Case Reports

Diabetic Lipemia With Fatty Splenomegaly Culminating in Unnecessary Splenectomy

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ELECTIVE SPLENECTOMY is usually undertaken for staging lymphomas, treating cytopenia or for mechanical reasons. Occasionally splenectomy is needed for the diagnosis of splenomegaly of obscure cause.[1]

A patient presenting with uncontrolled diabetes mellitus, lipemia and splenomegaly in the absence of abdominal pain underwent a diagnostic splenectomy. Preoperatively, an unusual feature of hyperlipoproteinemic splenomegaly—low-grade hemolysis—was present. In retrospect, fatty infiltration should have been considered as the cause of persistent splenomegaly. It is rational to observe such patients during effective lipid-lowering therapy before a diagnostic splenectomy is undertaken.

Report of a Case

The patient, a 58-year-old man, had a 13-year history of neglected non-insulin-dependent diabetes mellitus with sensory neuropathy and erectile dysfunction. He also had long-standing essential hypertension, hypertriglyceridemia, gout and obesity. He followed no diet, took 40 units of isophane (NPH) insulin and 20 units of crystalline zinc insulin in a single daily injection and was receiving clonidine, triamterene, hydrochlorothiazide, indapamide and allopurinol. Six months earlier a regimen of probucol, 500 mg twice a day, was begun "to lower cholesterol." One sister, aged 86, was reported to have diabetes, gout and hypertriglyceridemia. Another sister died of myocardial infarction at age 58.

Background diabetic retinopathy was present; lipemia retinalis, xanthomatosis and hepatomegaly were not observed. The spleen was palpable 6 to 8 cm below the left costal margin. Touch sensation was diminished over the feet and ankles.

Laboratory studies elicited the following values: serum sodium was 126, potassium 3.9, chloride 91 and bicarbonate 26 mEq per liter; glucose was 450, urea nitrogen 30, creatinine 1.7 and uric acid 10.2 mg per dl. Serum levels of aminotransferases, bilirubin and alkaline phosphatase were all normal. A fasting plasma cholesterol was 292 and triglycerides were 7,728 mg per dl. The plasma was not examined for chylomicronemia.

A blood leukocyte count was 3.7 to $5.0 \cdot 10^3$ per μl, platelets 1.2 to $1.3 \cdot 10^5$ per μl and packed red cell volume 47%. A modest reticulocytosis (3.9% to 4.8%) was seen (Figure 1). Occasional spherocytes were observed in the peripheral blood smear. Coombs' and osmotic fragility tests and a serum protein electrophoresis were normal. A specimen of bone marrow showed a normal number of megakaryocytes with erythroid hyperplasia and vacuolated reticuloendothelial cells (Figure 2).

After two weeks of a regimen of twice-a-day insulin (NPH and regular insulin, 30 and 15 units in the morning and 14 and 10 units in the evening, respectively) and a 2,000-kcal American Diabetes Association diet, the plasma cholesterol level was 223 mg per dl and triglycerides 690 mg per dl. Chylomicronemia was absent. Ultracentrifugation and electrophoresis of a plasma specimen taken with the patient in a fasting state showed elevated very-low-density-lipoprotein levels with greatly decreased levels of low- and high-density lipoproteins (type IV hyperlipoproteinemia).

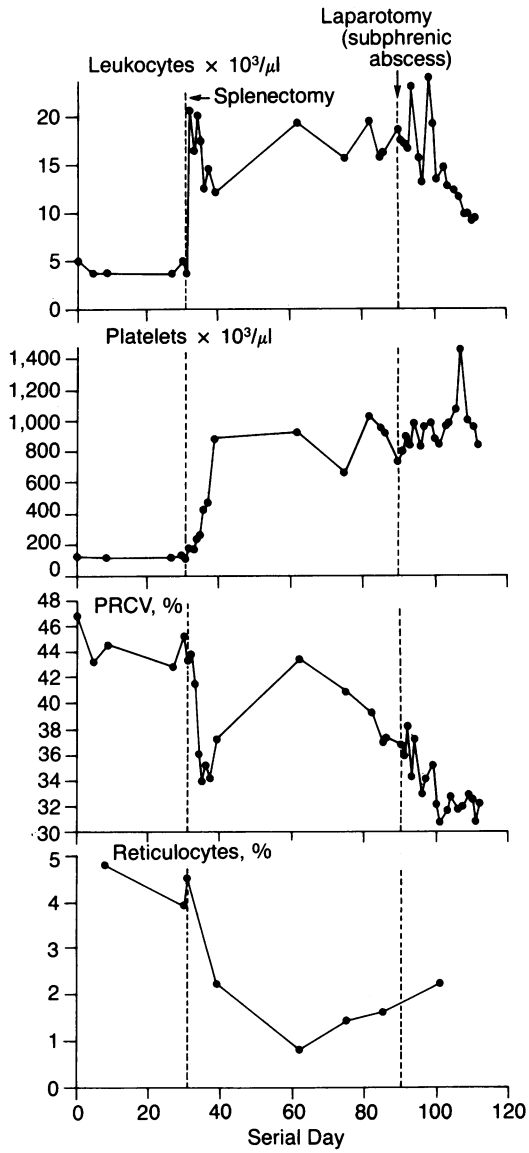

Figure 1.—The graphs show the clinical course of the patient before and after a splenectomy. PRCV = packed red cell volume

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At laparotomy four weeks after admission, the spleen weighed 850 grams. Hematoxylin and eosin-stained sections showed foamy histiocytes that stained positively with Sudan black and oil red O. Electron micrographs showed vacuolated foam cells (Figure 3). No lamellated or tubular bodies or ceroid was seen.

Reticulocyte counts fell to 0.8% to 2.2% in the postoperative period (Figure 1). Seven weeks after discharge, the patient presented with fever, chills and weight loss. A left subphrenic abscess was drained. Moderate hypertriglyceridemia (300 to 628 mg per dl) with decreased high-density-lipoprotein cholesterol (32.5 mg per dl) persisted. Two years after splenectomy, hematologic indices were normal, hemoglobin A_{1C} was 6.3% and there was a draining sinus in the splenectomy scar.

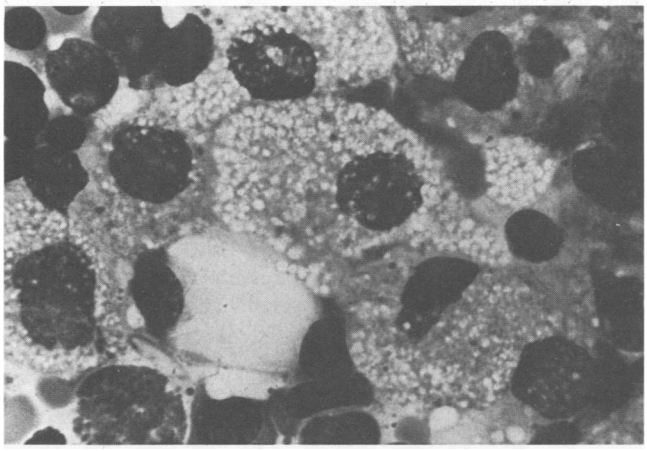

Figure 2.—Histologic examination of a bone marrow specimen (Giemsa stain) shows vacuolated reticuloendothelial cells (original magnification × 1,000).

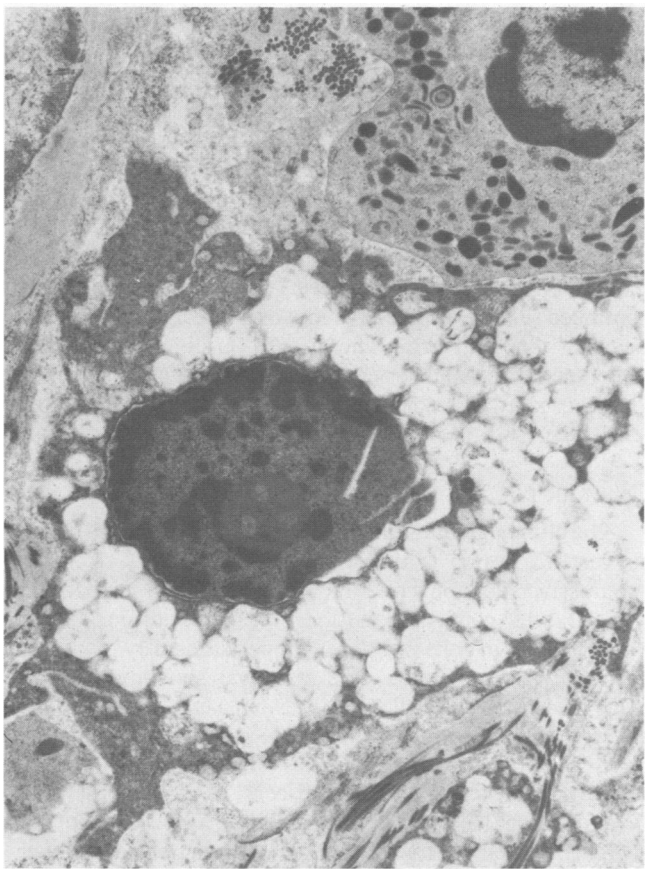

Figure 3.—Electron microscopy of a specimen of spleen shows macrophages with numerous vacuoles containing granular material staining less densely than neutral fat (original magnification × 4,000).

Discussion

Hyperlipoproteinemia with hypertriglyceridemia and chylomicronemia (types I and V) is a recognized cause of hepatosplenomegaly,[2,3] yet standard textbooks usually fail to include it among the causes of splenomegaly. In this patient, splenomegaly was not associated with an abdominal pain crisis, the clinical context in which it has most often been reported.[2] It is likely that chylomicronemia was present initially when the fasting triglyceride concentration exceeded 7,000 mg per dl, but the severe hypertriglyceridemia remitted promptly during treatment, diverting attention from lipemia as a cause of splenomegaly. Thus, when lipoprotein analysis was done two weeks after admission, the patient showed type IV hyperlipoproteinemia.

The significance of vacuolated reticuloendothelial cells in the bone marrow aspirate was not appreciated preoperatively; the correct diagnosis became clear only after foamy macrophages were noted on histologic examination of the spleen. In retrospect, a splenectomy and its resulting complications might have been avoided.

Diabetic lipemia, of which this patient had typical features, occurs when uncontrolled diabetes and an inherited disorder of lipoprotein metabolism coexist.[4] The patient had also received several drugs known to increase plasma triglyceride concentrations.[5] He probably had had long-standing chylomicronemia at the time of presentation. With severe chylomicronemia, the spleen, liver and bone marrow accumulate macrophage-derived foam cells engorged with lipid droplets and ceroid.[6]

Fatty splenomegaly was associated with hematologic abnormalities. Reticulocytosis in the absence of blood loss along with erythroid hyperplasia of the bone marrow and low-normal leukocyte and platelet counts was consistent with splenic sequestration of the cellular elements of blood. Blood loss and subphrenic abscess with inflammation undoubtedly contributed to postoperative anemia.

Successful treatment of diabetic hypertriglyceridemia requires control of hyperglycemia, reduction of excessive body weight and drug therapy in selected patients.[7] The use of probucol was inappropriate in the present case because it is ineffective for treating hypertriglyceridemia and often reduces plasma high-density-lipoprotein concentrations.[8] Furthermore, there is evidence from experiments in rabbits that probucol diverts lipoproteins from their normal catabolism through the low-density-lipoprotein (apoB,E) receptor to non-receptor-mediated catabolic pathways.[9] Thus, it is possible that administering probucol contributed to reticuloendothelial lipid deposition in this patient.

Correction of severe hypertriglyceridemia usually results in a reduction in the size of an enlarged fatty spleen. Patients with severe hypertriglyceridemia and otherwise unexplained splenomegaly deserve observation during effective lipid-lowering treatment before a diagnostic splenectomy is undertaken.

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Tuberculoma of the Brain Stem

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IN NORTH AMERICA, tuberculosis rarely involves the central nervous system (CNS). In developing countries, CNS manifestations of tuberculosis are more common. Patients may present with tuberculous meningitis, tuberculoma, tuberculous abscess and Pott's disease.[1] Tuberculomas are thought to occur most frequently in children.[1,2] Although potentially curable, tuberculomas often present a diagnostic puzzle, and the diagnosis may not be considered early in a patient's course. When a tuberculoma occurs in the brain stem, early diagnosis is critical if the patient is to survive. In Europe the incidence of intracranial tuberculoma may be increasing, partly because of an increasing number of refugees from developing countries.[2] The increasing inflow of refugees into the southwestern United States compels us to alert US physicians to this rare but curable lesion.

Report of a Case

At the time of presentation, the patient, a 70-year-old right-handed Cambodian woman, complained of slowly progressive nausea, vomiting, unsteady gait and double vision over three months. She had lost 9 kg (20 lb); a purified protein-derivative (PPD) skin test was reportedly positive in the past. She had no history of a transient ischemic attack, stroke, seizure or known cancer. She had lived in San Diego four years, having moved from Cambodia. She was taking no medications other than prochlorperazine for nausea. The patient was cachectic but there were no other findings on general medical and gynecologic examinations. On examination through an interpreter, her mental state was normal. On the left, there was a mild sixth nerve paresis and a mild lower motor neuron-type facial paresis. The other cranial nerves were normal. On motor testing, the right upper and lower extremities were mildly weak. Appreciation of pin, touch, vibration and position was moderately diminished in the right upper extremity and slightly diminished in the right lower extremity. Reflexes were present and symmetric with downgoing toes. There was an intention tremor in the right arm and leg. The patient was unable to stand because of ataxia; on sitting there was truncal titubation.

ABBREVIATIONS USED IN TEXT

CNS = central nervous system
CSF = cerebrospinal fluid
CT = computed tomography
ESR = erythrocyte sedimentation rate
PPD = purified protein derivative

The patient was admitted to the hospital for a presumed left pontine mass lesion and the following studies elicited no abnormalities: complete blood count, electrolytes, calcium, liver function tests, thyroid function tests, serum B_{12} level, coagulation studies, urinalysis, arterial blood gas determinations, intravenous pyelogram, liver-spleen scan and abdominal ultrasonogram. A bone scan was abnormal at the site of an old trauma in three ribs on the right. An erythrocyte sedimentation rate (ESR) was 47 mm per hour. Skin tests were negative for PPD and positive for mumps and *Candida*. A computed tomographic (CT) head scan with and without contrast infusion showed a round enhancing lesion in the pons, with mass effect and surrounding edema (Figure 1). A lumbar puncture produced a clear colorless fluid under normal pressure with a glucose concentration of 46 mg per dl (concurrent serum glucose level, 98 mg per dl), protein 41 mg per dl, 2 lymphocytes and 1 erythrocyte per μl. Smears and cultures for fungi, bacteria, acid-fast bacilli and cytologic examination were normal. Bone marrow aspiration failed to produce acid-fast bacilli on smears and cultures. A cerebral angiogram confirmed the presence of an avascular mass in the pons.

Treatment with dexamethasone, isoniazid, rifampin, ethambutol hydrochloride and pyridoxine hydrochloride was begun. After two weeks the patient's condition had improved to the point that she was no longer vomiting, could ambulate with no assistance and showed nearly normal strength on the right. Her left sixth nerve paresis and diplopia persisted. Over the ensuing months she continued to show slow improvement, and after 18 months the antitubercular therapy was stopped; the dexamethasone dosage was tapered 20 months after presentation. When last examined, the patient continued to have a subjective loss of appreciation of pin and touch in the right arm. There were no objective sensory, motor, reflex, cranial nerve or cerebellar findings. Follow-up CT scans showed resolution of the mass and persistence of a small lucency in the pontine tegmentum.

Comment

The clinical findings in the patient presented herein clearly suggested a lesion in the left pons. The history of slowly progressive symptoms over months suggested a mass lesion. The CT scan confirmed the location of the lesion, and the enhancement pattern suggested hypervascularity or blood-brain-barrier breakdown. The mass was shown to be avascular on angiography. Thus, the lesion was a solitary, round, avascular mass with significant blood-brain-barrier breakdown. The cerebrospinal fluid (CSF) findings essentially ruled out bacterial or parasitic abscess, as did the absence of fever or serum leukocytosis. A primary malignant tumor was searched for but not found. The patient was treated for tuberculous granuloma, and the successful resolution of the lesion eliminated metastasis, fungal abscess and other granulomatous disease as possibilities.

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